UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/088,748	07/19/2002	Martin Friede	B45226	8803

20462 7590 03/25/2004

SMITHKLINE BEECHAM CORPORATION
CORPORATE INTELLECTUAL PROPERTY-US, UW2220
P. O. BOX 1539
KING OF PRUSSIA, PA 19406-0939

EXAMINER	
LUCAS, ZACHARIAH	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 03/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/088,748	FRIEDE ET AL.	
	Examiner	Art Unit	
	Zachariah Lucas	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *33-64* is/are pending in the application.

4a) Of the above claim(s) *64* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *33-63* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/20/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I, subgroups 1 and A, and the species wherein the surfactant is t- octylphenoxypolyethoxyethanol (Triton X-100) in the paper filed on December 19, 2003 is acknowledged. The traversal is on the ground(s) that the inventions are linked by the special technical feature of administering any non-live viral antigen. This is not found persuasive because the special technical feature is disclosed in the prior art. See e.g., Glück et al., J Virol 73(9): 7780-86, disclosing the intranasal administration of an influenza antigen meeting the structural limitations of certain preferred embodiments. It is noted that, although the claims indicate that a one dose viral antigen preparation is being administered, the claimed method does not exclude multiple administrations of the preparation. Because the current claims do not distinguish over the prior art, the claims are not linked by a special technical feature. Thus, although claim 33 is a linking claim, the Applicant has not demonstrated that the multiple inventions share a common special technical feature in the preparation being used. Claims 33-63 will therefore be examined to the extent that they read on the elected invention.

The requirement is still deemed proper and is therefore made FINAL.

2. Claim 64 is withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the paper filed December 19, 2003.

Information Disclosure Statement

3. The information disclosure statement (IDS) submitted on March 20, 2002, is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement has been considered by the examiner.

4. The following reference is an English abstract of a foreign language document. Due to this, the reference has been examined only to the extent of the disclosure in the abstract.

Reference CA in the IDS, (Berdnikova et al), abstract of application 1994RU-002944.

5. The following reference is in a foreign language accompanied by an English abstract. Due to this, the reference has been examined only to the extent of the disclosure in the abstract.

Reference BC in the IDS, WO 00/4722.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 33-44, 48, 50-63 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. These claims read on methods for the prophylaxis of influenza infection in a subject comprising administering to the subject a one-dose intranasal non-live influenza vaccine that generates an immune response meeting the requirements of international regulatory requirements. However, it is not clear from the application how the presently claimed influenza vaccines differ from the vaccines of the prior art. While the Applicant has indicated that the vaccines are "one dose" vaccines, they have provided little guidance as to what structural

or formulation characteristics distinguish such vaccines from those in the art. For example, while the application indicates on page 14 that "[a]dvantageously, a vaccine dose according to the invention is provided in a smaller volume than a the conventional injected split flu vaccines, which are generally 0.5 or 1 ml per dose." The specification further states "The low volume doses according to the invention are preferably below 500 µl, more preferably below 300 µl and most preferably not more than about 200 µl or less per dose." Id. However, while the application indicates that the vaccine formulation either "advantageously" or "preferably" falls within these ranges, it does not set any specific limitations on the formulation of the one dose vaccines used in the claimed methods. It is therefore unclear what constitutes a "one-dose intranasal non-live influenza vaccine" according to the present invention. It is not clear if there are, in fact, any structural or formulation differences between the vaccines used in the claimed methods, and those of the prior art, or if the claims broadly include any vaccine formulation, including those in the prior art, that would achieve the required results. Clarification is required.

8. Claims 34 and 35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims read on the claimed methods, wherein administration of the one-dose preparation achieves at lest two out of three of the European Union criteria "for the or all strains of influenza present in the one-dose intranasal preparation." It is not clear what is meant by the phrase "for the or all." Clarification of the claim language is required.

9. Claims 38-42 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 38 recites the limitation "wherein the formulation comprises..." There is insufficient antecedent basis for this limitation in the claim. The claim from which claim 38 depends, claim 33, recites a one-dose antigen preparation, but does not refer to this preparation as a formulation. For the purposes of this action, it is assumed that the formulation of claim 38 refers to the preparation of claim 33. However, clarification as to what formulation is actually being referred to is required.

10. Claim 39 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In the parenthetical statement after the term ocytlphenoxypolyethoxyethanol, the phrase "for example" renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d). It is also unclear if the parenthetical statement identifying the polyethylene sorbitan esters as from the Tween TM series is indicating that only Tween products are included in the claim language. It is suggested that the parenthetical remarks be removed from the claim.

11. Claim 43 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claim reads on the claimed method wherein the antigen preparation includes a bile or cholic acid, "or derivative thereof such as sodium deoxycholate." The phrase "such as"

renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d). Specifically, it is unclear if the phrase "such a sodium deoxycholate" is intended to limit the term "derivative" to the specific compound disclosed in the phrase. It is suggested that the phrase be deleted from the claim.

12. Claims 44, 48, and 61 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. These claims each include a phrase such as "wherein each does of the vaccine formulation contains a low dose of haemagglutinin" or "wherein the vaccine formulation is in a low volume per dose." The term "low" in these claims is a relative term which renders the claim indefinite. The term "low" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The claims are therefore indefinite because it is not clear what formulations fall within the claimed limitations.

13. Claim 49 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by

"such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 49 recites the broad recitation "wherein the volume per dose is less than 500 μl, and the claim also recites "or less than 300μl or not more than about 200μl" which represents two narrower statements of the range/limitation. Thus, the claim is indefinite as it is not clear what the dosage volume is intended to be.

14. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

15. Claims 33-63 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods wherein two or more administrations of the indicated antigen preparations or where a single administration of the preparations disclosed in examples 4 and 5 of the application are provided to a patient such that an immune response meeting the international regulatory requirements for influenza vaccines are met, does not reasonably provide enablement for methods where any single administration is made. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. The claims read

on methods of administering a one-dose intranasal non-live influenza virus antigen preparation wherein the single dose meets the international regulatory requirements for influenza vaccines. In particular, the Applicant is not enabled for the methods wherein dosages of less than 30 μg of HA are provided or where the vaccine does not include an immunostimulant.

In making a determination as to whether an application has met the requirements for enablement under 35 U.S.C. 112 ¶ 1, the courts have put forth a series of factors. See, In re Wands, 8 USPQ2d 1400, at 1404 (CAFC 1988); and Ex Parte Forman, 230 U.S.P.Q. 546 (BPAI 1986). The factors that may be considered include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. Id. While it is not essential that every factor be examined in detail, those factors deemed most relevant should be considered.

In the present case, as indicated by the Applicant, the prior art teaches that the administration of a single dose of intranasal influenza antigen preparations is insufficient to meet the stated requirements for influenza vaccines. App., pages 3-6. The Applicant notes the teachings of several references in these pages demonstrating that the administration of single doses of intranasal influenza antigen preparations to humans was insufficient to induce these requisite immune responses. As noted by the Applicant, the art teaches in order to effectively use intranasal antigen preparations against influenza multiple administrations of the intranasal formulations are required, the preparations should include an immunostimulant, and that greater dosages (than 15 μg) of HA are necessary.

In contrast to these teachings in the art, the Applicant has, on pages 32-33 and 36-38 demonstrated that a particular antigen preparation was effective in meeting the indicated regulatory requirements. The only formulations tested in humans were the formulation of examples 4 and 5, which formulations comprise HA contents of 30 μg and multiple immunostimulants. Thus, while the Applicant also demonstrated that other single dosages were effective at raising immune responses in mice, in view of the teachings in the prior art that such intranasal dosages have been insufficient in humans, the Applicant has not demonstrated that any low dose intranasal influenza preparation, particularly those without an immunostimulant, would meet the regulatory requirements in humans. This is because the conflict between the teachings in the prior art and those in the mouse models of the present specification indicates that there may be some unpredictability, or complexity, in the predication of particular preparations' ability to induce the required response in humans. Therefore, while the Applicant appears to be enabled for one-dose administrations of the formulations in examples 4 and 5, and for administration of multiple dosages of preparations with 15 μg, the application is not enabling for methods of inducing the requisite immune responses with a single administration of any influenza antigen preparation.

Claim 47 is further rejected because the teachings in the application do not provide evidence that dosages of 7.5 μg HA in the absence of an immunostimulant would be effective for the induction of the requisite immune responses. The Applicant has demonstrated in mice that preparations with lower dosages of HA is effective in mice to induce comparable immune responses to those required by the international regulations. However, in addition to the teachings in the art indicating that such low dosages may not be effective in humans, the

Applicant has not demonstrated that dosages of .75 μg (murine equivalent dosage to 7.5 μg in humans) would be effective in the induction of the requisite immune response where the antigen is not administered in combination with an immunostimulant.

Because the teachings of the present application are not sufficient to overcome the teachings in the art that any single dose formulation of influenza antigen preparation would be effective in the claimed methods, the Applicant is not enabled for the full scope of the claimed inventions.

16. Claims 33-63 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims have been described above. They describe a genus of inventions comprising methods of administering any one-dose intranasal non-live influenza virus preparation wherein that preparation is capable, after a single administration, of meeting the functional requirements indicated in (e.g.) claim 55.

The following quotation from section 2163 of the Manual of Patent Examination Procedure is a brief discussion of what is required in a specification to satisfy the 35 U.S.C. 112 written description requirement for a generic claim covering several distinct inventions:

> The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice..., reduction to drawings..., or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus... See Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406.

> A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

Thus, when a claim covers a genus of inventions, the specification must provide written description support for the entire scope of the genus. Support for a genus is generally found where the applicant has provided a number of examples sufficient so that one in the art would recognize from the specification the scope of what is being claimed. However, the Federal Circuit has also indicated that an inventor of "a biotechnological invention cannot necessarily claim a genus after only describing a limited number of species because there may be unpredictability in the results obtained from species other than those specifically enumerated." Noelle v. Lederman, 69 U.S.P.Q. 2d 1508 (Fed Cir, No. 2004). The Federal Circuit has therefore indicated both that sufficient teachings be present in the application to indicate to those in the art that the Applicant is in possession of the full scope of the claimed genus, and that, even where the Applicant has demonstrated possession of a number of species, the Applicant may not be entitled to claims to the entire genus where the operability of other species is unpredictable.

In the present case, the Applicant has provided a working example of the claimed invention (the formulation of examples 4 and 5). However, as was indicated above, the application does not provide any formula or structural limitations on the contents of the one dose antigen preparations of the claims such that they may be distinguished from those in the prior art by means other than the immunogenic response. It is noted that the Applicant has provided additional guidance as to potentially effective vaccine formulations in the examples involving murine models. However, as was also indicated above, and in the application, the prior art teaches that not every influenza vaccine preparation that falls within the scope of the claimed

formulations satisfies the functional language of the claims. Given the conflict between the teachings of the prior art (evidence that low dose intranasal formulations are not adequate to meet the claimed functions when administered to humans) and the teachings in the present application (in mouse models), there is some unpredictability in the performance of the one dose vaccines in humans. Thus, given the single working example, the apparent unpredictability in the art, and the limited guidance in the application towards other operative embodiments, the Applicant has not provided sufficient information in the application to demonstrate that the Applicant was in possession of the full scope of the claimed genus at the time of filing.

Claim Rejections - 35 USC § 102

17. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

18. Claims 33-38, 44-48, 50, 51, and 55-59 are rejected under 35 U.S.C. 102(b) as being anticipated by Oh et al., Vaccine 10(8): 506-11. The claims have been described above. Oh teaches the intranasal administration to humans of a commercially available influenza vaccine composition. Oh teaches the administration to humans an intranasal aerosol form of a split-antigen influenza vaccine. Page 507. The reference teaches that the vaccine is delivered by way of an aerosol spray, with one half dose being administered into each nostril. Id. It is noted that

the reference does not teach the relationship of the results achieved by the administration with respect to the international standards. It is further noted that the reference teaches that multiple doses of the vaccine are administered. However, this is not deemed to distinguish over the claimed invention because the claims do not exclude the administration of additional dosages, and because the Applicant has not distinguished the "one-dose" vaccines from that used by Oh. Because it appears that Oh is administering a vaccine such as is being administered in the claimed method, the intended results of the claimed method do not distinguish over the disclosed vaccine administrations. See, MPEP 2114. The claims are therefore anticipated by the teachings of Oh.

19. Claims 33-38, 43-49, 51, and 55-58 are rejected under 35 U.S.C. 102(a) as being anticipated by the teachings of Glück et al., J Virol (supra). The claims have been described in part above. Claims 47-49 further limit the haemagluttinin content and volume of the antigen preparations. As indicated above, no other description of the "one dose intranasal non-live influenza virus antigen preparation[s]" used in the claimed methods has been provided. Further, because the claims indicate that the methods *comprise* an administration of the one dose preparation, the claims are mot limited to methods where only a single dose of the preparation is administered. While claims 55-58 do indicate that the method "comprises administering to the subject a single dose" of the vaccine, the claims do not require that no further doses be administered. Thus, the claims are not read as requiring only a single dose of vaccine administration.

Glück teaches the intranasal administration of influenza antigen formulations comprising either 7.5 or 15 μg of haemagluttinin per 200 μl dose, with one 7.5 μg formulation not comprising an adjuvant. The reference discloses that the antigen is prepared by chemically disintegrating virus particles. Pages 7780-81. Thus, the reference teaches the use of split-antigen viral preparations. The reference also discloses the administration of the 7.5 μg formulations twice, and the single administration of a concentrated version of the 15 μg formulation. Thus, the reference teaches the methods described by the rejected claims.

Claim Rejections - 35 USC § 103

20. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

21. Claims 38-40, and 52-54 are rejected under 35 U.S.C. 103(a) as being unpatentable over either Oh or Glück as applied above, and further in view of Friede et al. (WO 99/52549- of record in the March 2002 IDS) These claims further limit the claimed methods to those wherein the one-dose anti-influenza preparations comprise the surfactant laureth 9, and/or the immunostimulant 3D-MPL. The teachings of Glück have been described above. While the reference teaches a method of inducing an immune response using an anti-influenza vaccine for mucosal administration, the reference does not teach the use of the particular surfactants or the immunostimulant 3D-MPL.

However, Friede provides teachings regarding adjuvant compositions for use in mucosal vaccines. Page 1. Included in these teachings is the use of non-ionic surfactants, including lauryth 9 (polyoxyethylene-9 lauryl ether) in such compositions. See, pages 2-4, esp. page 4. The reference also teaches the use of adjuvants in the vaccine formulations, especially in combination with the surfactants. Page 7. Included among the suggested adjuvants and immunostimulants are monophosphoryl lipid A, and its derivative 3D-MPL. Page 7. The reference therefore teaches the use of both lauryth 9 and 3D-MPL, alone or in combination, in mucosal vaccines. It would therefore have been obvious to those in the art to use these compounds in formulations comprising the antigens for intranasal vaccination disclosed by Glück.

22. Claims 38-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over either Oh or Glück in view of Friede as applied to claims 38-40, and 52-54 above, and further in view of either Baker et al. (U.S. 6,506,803) or Morein et al. (U.S. 5,679,354). The claims have been described above, except that the presently rejected claims require that the antigen preparation include one or both of the surfactants Triton X-100 or Tween 80. As indicated above, Friede teaches that non-ionic surfactants may be beneficially used in vaccine formulations, including those for mucosal administration. Each of Baker and Morein also teach that these surfactants have utility, and even immunostimulating activity, in immunogenic compositions, and suggest Triton X-100 and Tween 80 as such surfactants. See, Baker, columns 10-11; and Morein, column 4, lines 38-62. Because these detergents are known in the art to be usable in immunogenic compositions, and because the references suggest the use of these compounds in vaccine

formulations, it would have been obvious to those in the art to use one or more of these detergents in anti-influenza preparation such as the ones disclosed in Glück and those claimed.

23. Claims 50, and 61-63 are rejected under 35 U.S.C. 103(a) as being unpatentable over either Oh or Glück as applied to claims 33-36, 38, 43-49, 51, and 55-58 above, and further in view of either of Baum et al. (U.S. 3,874,381) or Weinstein et al. (U.S. 5,437,267). These claims further describe the methods and kits described above, wherein the methods involves the administration of two subdoses of the vaccine, or the inclusion of an intranasal delivery device. Glück does not teach or suggest such limitations.

However, the Baum and Weinstein reference each teach devices for intranasal delivery of compositions, including medications. Because the vaccine disclosed by Glück is intended for intranasal delivery, and Baum or Weinstein disclose devices for the delivery of such compositions, it would have been obvious to those in the art to use the devices of these references to administer the vaccine. As these devices would inherently administer two subdoses, one to each nostril, the limitations of the indicated claims would also have been obvious to those in the art.

24. Claims 60-63 are rejected under 35 U.S.C. 103(a) as being unpatentable over the teachings of Barrett et al. (WO 00/47222) in view of either Baum or Weinstein as applied against claims 50, and 61-63 above. For the purposes of this rejection, reference will be made to U.S. Patent 6,635,246, which is a U.S. Patent in English filed from the international application

published in German as WO 00/47222. These claims read on a kit comprising an intranasal delivery device and a one-dose intranasal anti-influenza vaccine.

Barrett teaches an anti-influenza preparation for influenza vaccination comprising an adjuvant and an influenza virus antigen administered at a dose of between 1.5 and 50 μg per dose, and in particular, teaches a formulation comprising 15 μg per dose. See, column 3 lines 17-21, and col. 4 lines 48-55 (corresponding to the WO publications' teachings on pages 4 and 7). Barrett does not teach the inclusion in a kit of both the antigen formulation and a delivery device. However, because the reference indicates that the formulations can be administered intranasally, it would have been obvious to those in the art to include in a kit comprising the formulation an intranasal delivery device such as those taught Baum or Weinstein.

It is noted Barrett does not teach the antigen formulations disclosed therein as one-dose vaccines. However, as was noted above, the Applicant has not provided any means by which to structurally distinguish the claimed compositions from those described in the art. Thus, because the formulations of Barrett appear to meet the structural limitations of the claimed inventions, the formulations in the reference would inherently have the functional characteristics of those inventions. The combination of Barrett and Baum or Weinstein therefore teaches all of the limitations of the claimed invention, and renders the claimed kits obvious.

25. Claims 59-63 are rejected under 35 U.S.C. 103(a) as being unpatentable over the teachings of Chatfield (WO 97/16208) in view of Barrett, Baum, Weinstein as applied against claims 61-63 above. Claim 59 teaches that the kit described above includes a non-live influenza antigen preparation that does not include an added immunostimulant. The teachings of Barrett,

Baum, and Weinstein have been described above. These references do not teach that the antigen preparation does not include an immunostimulant.

Chatfield teaches a kit comprising an influenza antigen preparation in a first container, an immunostimulant in a second container, and a delivery device. See, pages 5-6. Thus, the reference teaches a kit comprising a non-live influenza vaccine preparation without an adjuvant and a delivery device. The reference therefore teaches the claimed kits for substantially the same reasons as indicated with respect to the Barrett/Baum/Weinstein references above. However, the reference does not alone teach the devices as required by claim 62, or that the dose is less than 30 μg (which appears to constitute a low dose vaccine). Chatfield does teach that the antigen compositions preferably comprise between 1 and 50 μg of protein from each of the virus strains in the vaccine. Page 7. This range is equivalent to the range disclosed by the Barrett reference, which further indicates that inclusion of 15μg is an acceptable amount of protein from each virus. Thus, it would have been obvious to those in the art to include in the kits of Chatfield antigen preparations comprising 15 μg of HA from each influenza strain, and a device such as those disclosed in either Baum or Weinstein. These references therefore render obvious to the kit of claims 59-63.

Conclusion

26. No claims are allowed.

27. The following prior art references are made of record and considered pertinent to applicant's disclosure. However, while relevant they are also not used as a basis for rejection for the stated reasons.

Gross et al., J Clin Microbiol, 14(5): 534-38. This reference teaches the intramuscular administration of a split-influenza vaccine comprising 7 μg of HA from each of the viral serotypes included in the vaccine. The reference does not teach or suggest the administration of the vaccine through intranasal routes.

Kumo-Sakai et al., Vaccine 12(14): 1303-10. This reference teaches that, although upper respiratory tract administration of influenza vaccines were previously believed to be inferior to subcutaneous routes, certain benefits are achieved using the respiratory tract routes over the subcutaneous routes. Abstract. The teachings of this reference are deemed duplicative to those of Oh above.

28. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 571-272-0905. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Z. Lucas
Patent Examiner

James C. Housel 3/22/04
JAMES HOUSEL
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600